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08/984,476	12/03/97	WOLFE	M 34477.2

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EXAMINER

ROMEO, D

ART UNIT	PAPER NUMBER
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1647

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DATE MAILED:

09/05/00

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trad marks**

# Office Action Summary

Application No.  
**08/984,476**

Applicant(s)  
**Wolfe et al.**

Examiner  
**David S. Romeo**

Group Art Unit  
**1647**



☒ Responsive to communication(s) filed on 19 Jul 2000

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

## Disposition of Claims

☒ Claim(s) 1, 8-16, and 18-42 is/are pending in the application.

Of the above, claim(s) 42 is/are withdrawn from consideration.

☐ Claim(s) \_\_\_\_\_ is/are allowed.

☒ Claim(s) 1, 8-16, and 18-41 is/are rejected.

☐ Claim(s) \_\_\_\_\_ is/are objected to.

☒ Claims 1, 8-16, and 18-42 are subject to restriction or election requirement.

## Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some\* ☐ None of the CERTIFIED copies of the priority documents have been  
☐ received.

☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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### DETAILED ACTION

1. The request filed on 07/19/00 (Paper No. 14) for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08984476 is acceptable and a CPA has been established. An action on the CPA follows.

2. Claims 1, 8-16, 18-42 are pending. The originally presented invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 42 remains withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

3. Claims 1, 8-16, 18-41 are being examined.

4. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

In the "APPLICATION FOR A U.S. PATENT TRANSMITTAL FORM" submitted 12/30/97 it is stated that the application claims the benefit under 35 USC 119(e) of U.S. provisional application no. 60/032,329. However, the oath or declaration does not make such a

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claim. Applicants are required to submit a substitute oath or declaration identifying the provisional application for which claimed benefit is desired.

5. A substitute specification including claims is required pursuant to 37 CFR 1.125(a) because the interlineations and/or cancellations made in the specification or amendments to the claims make the application difficult to consider and could lead to confusion and mistake during examination and/or during the issue and printing processes. .

A substitute specification filed under 37 CFR 1.125(a) must only contain subject matter from the original specification and any previously entered amendment under 37 CFR 1.121. If the substitute specification contains additional subject matter not of record, the substitute specification must be filed under 37 CFR 1.125(b) and must be accompanied by: 1) a statement that the substitute specification contains no new matter; and 2) a marked-up copy showing the amendments to be made via the substitute specification relative to the specification at the time the substitute specification is filed.

6. Claim 16 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the

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claim(s) in independent form. A reconstituted antagonist does not infringe a lyophilized antagonist.

7. The amendment filed 04/16/99 (Paper No. 5) is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall  
5 introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The specification does not provide a basis for a GIP antagonist wherein the GIP antagonist is a fragment of human GIP. The disclosure of human GIP is in the context of immunogenic peptides to be used for the production of antibodies (paragraph bridging pages 7-8). This objection under 35 U.S.C. 132 encompasses the sequence  
10 listing, including SEQ ID NOs:4, 6, 13, which are described as human. Deleting "human" would overcome the objection to SEQ ID NOs:4, 6, 13.

Applicant is required to cancel the new matter in the reply to this Office action.

***Claim Rejections - 35 USC § 112***

8. Claims 1, 9, 10, 12, 13, 23, 24, 27-32, 35-40 are rejected under 35 U.S.C. 112, first  
15 paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. A

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basis for the following limitations cannot be found in the specification or claims as originally filed:

a GIP antagonist comprising a human GIP fragment and/or wherein said human GIP antagonists

comprises SEQ ID NOs:2-6, 13; a polypeptide that interferes with the biological activity of GIP

wherein said polypeptide comprises an amino acid sequence corresponding to amino acids 16-30,

5 21-30, or 7-9 of GIP. The introduction of such limitations raises the issue of new matter.

9. Claims 1, 8, 9, 10, 11, 12, 15, 16, 18, 19 rejected under 35 U.S.C. 112, first paragraph,

because the specification, while being enabling for an antagonist of GIP consisting essentially of

amino acids 7-30 or 10-30 of rat GIP, does not reasonably provide enablement for an antagonist

of GIP without regard to the structure thereof, effective alternative sequences thereto, or for

10 antagonistic polypeptides comprising other than amino acids 7-30 or 10-30. The specification

does not enable any person skilled in the art to which it pertains, or with which it is most nearly

connected, to make the invention commensurate in scope with these claims. The instant

specification clearly contemplates GIP sequences that include additional, deleted or alternative

amino acids (page 7, lines 14-19). Antagonist that "correspond to" GIP include additional,

15 deleted or alternative amino acids thereto. The specification teaches that rat GIP<sub>7-30 and 10-30</sub> are

antagonist. However, the claims encompass all naturally and non-naturally occurring compounds

and/or polypeptides that have the desired activity. The instant specification does not identify

those amino acid residues in the amino acid sequence of an antagonist or effective alternative

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sequences thereto or the structural features of a non-peptide antagonistic compound which are essential for their biological activity and structural integrity and those residues and/or structural features which are either expendable or substitutable. In the absence of this information a practitioner would have to resort to a substantial amount of undue experimentation in the form of insertional, deletional and substitutional mutation analysis of over 24 amino acid residues and/or random, trial and error testing of all compounds before they could even begin to rationally design a functional antagonist having other than a natural amino acid sequence of rat GIP. The disclosure of a single antagonist with a natural amino acid sequence is clearly insufficient support under 35 U.S.C. § 112, first paragraph, for claims which encompass any and all antagonistic compounds.

The current claim limitations are analogous to those of claim 7 of U.S. Patent No. 4,703,008, which were held to be invalid under 35 U.S.C. § 112, first paragraph, for want of enablement in *Amgen Inc. v. Chugai Pharmaceuticals Co. Ltd.*, 18 USPQ 2d, 1016 (CAFC, 3/5/91, see page 1026, section D). In that instance a claim to a nucleic acid molecule encoding a polypeptide having an amino acid sequence sufficiently duplicative of the amino acid sequence of erythropoietin (EPO) so as to have a specified biological activity was held to be invalid under 35 U.S.C. § 112, first paragraph, for want of enablement. This limitation is directly analogous to the effective alternative sequences thereto limitation of the instant claims. The disclosure upon which that claim was based described a recombinant DNA encoding EPO and a few analogs thereof.

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That disclosure differs from the instant specification because, whereas the instant specification describes a single antagonist with a natural amino acid sequence, it does not describe even a single effective alternative sequence thereto. The court held that what is necessary to support claims of this breadth is a disclosure sufficient to enable one skilled in the art to carry out the invention commensurate with the scope of the claims. That means disclosing how to make and use enough sequences to justify the grant of the patent protection sought in the instant claims. As indicated, the instant specification is even more limited than the '008 patent because it describes only a naturally occurring amino acid sequence and no effective alternative sequences thereto and, therefore, provides even less support than the '008 specification for claims of comparable scope and which were held to be invalid in that patent.

The antagonist of claim 39 is only limited by amino acids 7-9 of GIP. The structure of the antagonist is unlimited beyond these three amino acids. The specification has only shown that peptides comprising amino acids 7-30 or 10-30 have antagonistic activity. The specification has not shown that amino acids 7-9 have antagonistic activity. Three amino acids are only ~13% of the structure of a 21-24 amino acid peptide. The reasonable expectation in the art would be that deleting 87% of a peptide's structure would result in a non-functional peptide. Moreover, the specification teaches that the peptide antagonists would appear to require amino acids 7-9 and some or all amino acids 10-30. Furthermore, the specification only teaches that the 7-30 and 10-30 fragments are antagonistic (page 13). The specification does not provide a reasonable



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expectation that peptides other than amino acids 7-30 or 10-30 would have the required activity.

The skilled artisan is left to extensive experimentation wherein peptides other than amino acids 7-30 or 10-30 are randomly modified and through trial and experimentation is left to determine

which peptides are functional. Such extensive, random, trial and error experimentation is

5 considered undue. Moreover, there is a lack of predictability in the art with respect to predicting structure, hence function, from primary amino acid sequence data. See Ngo (u12)<sup>1</sup> wherein it is taught that the native structure of a protein is a unique three-dimensional structure into which the protein folds under physiological conditions and all the information necessary to determine the native structure can be contained in the primary amino acid sequence (page 433, full paragraph 1).

10 However, it is not even known whether there exist an efficient algorithm for predicting the structure of a given protein from its amino acid sequence alone (page 492, full paragraph 2).

In view of the breadth of the claims, the limited amount of direction and working examples provided by the inventor, the unpredictability in the art and the quantity of experimentation needed to make or use the invention based on the content of the disclosure, it would require  
15 undue experimentation for the skilled artisan to make and use the full scope of the claimed invention.

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<sup>1</sup>References cited by the examiner are in an alphanumeric format, such as "a1", wherein the "a" refers to the reference cited on the Notice of References Cited, PTO-892, and the "1" refers to the Paper No. to which the Notice of References Cited, PTO-892, is attached.

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10. Claims 11-14, 20, 21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reducing glucose adsorption, does not reasonably provide enablement for preventing, inhibiting, or reducing obesity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The claims are drawn to a pharmaceutical composition useful for the preventing, inhibiting, or reducing obesity, which requires that the composition be able to so perform. The specification teaches that ANTIGIP reduced intestinal glucose adsorption (Example 6). However, neither the specification nor the prior art of record establishes a nexus between this activity and preventing, inhibiting, or reducing obesity. The specification fails to disclose specific guidance for administering a GIP antagonist and thereby preventing, inhibiting, or reducing obesity. There are no working examples of preventing, inhibiting, or reducing obesity. Marx (v12) states that few "medical problems have proved to be more intractable than obesity"; the condition is frustratingly hard to treat (page 1477, column 1, full paragraph 1). Woods (w12) teaches that although satiety peptides can alter the size of individual meals, their repeated administration does not alter body weight and has limited influence on adiposity (page 1379, column 1, full paragraph 2). In view of the intractable nature and unpredictability of treating obesity and the lack of guidance with respect to dosages and the lack of working examples, one skilled in the art could not use claimed pharmaceutical composition for preventing, inhibiting, or reducing obesity without undue experimentation.

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11. The following claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5 Claim 9 is rejected over the recitation of "posts 7-30 of the sequence" because the phrase makes no sense. The metes and bounds of the claim(s) are not clearly set forth.

Claims 9, 12, 18, 20, 23, 25, 27, 29, 31, 33, 35, 37 are indefinite over the recitation of "effective number of amino acids" because it is unclear what effect is achieved by the effective number. The metes and bounds of the claim(s) are not clearly set forth.

10 Claims 9, 10, 12, 13, 18-21, 23-38, 40, 41 are indefinite over the recitation of "effective alternative sequences" because it is unclear what effect is achieved by the effective alternative sequences. The metes and bounds of the claim(s) are not clearly set forth.

Claims 11-14, 20, 21 are indefinite because it is unclear if inhibiting, blocking, or reducing glucose adsorption is synonymous with preventing, inhibiting, or reducing obesity or whether some other effect is intended. The metes and bounds of the claim(s) are not clearly set forth.

15 Claims 22, 39 are indefinite over the recitation of "effective amount" because it is unclear what effect is intended by an "effective amount"; an intended use is not the same as an effect; in the absence of a recitation as to any effect, or an effective amount of the agent to cause an effect, it is unclear what effect can be inferred.

Claims 22-41 are indefinite over the recitation of the acronym "GIP" because its meaning is ambiguous. The acronym could also be formed from the amino acid sequence glycine-isoleucine-proline. It is suggested that the acronym be spelled out at its first occurrence in claims 22 and 39.

The instant specification clearly contemplates GIP sequences that include additional, deleted or alternative amino acids (page 7, lines 14-19). Antagonist that "correspond to" GIP include additional, deleted or alternative amino acids thereto. Claim(s) 1, 9, 10, 12, 13, 18-21, 23-41 are indefinite because they recite the term "corresponding to". Because the instant specification does not identify that material element or combination of elements which is unique to, and, therefore, definitive of "corresponding to" an artisan cannot determine what additional material and/or functional limitations are placed upon a claim by the presence of this term.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5        13.        Claims 1, 8, 9, 10, 18, 19, 22-41 are rejected under 35 U.S.C. 102(a) as being anticipated  
by Gelling (x12). The instant application and the 60032329 provisional application only provide a  
basis for rat ANTIGIP. Gelling teaches porcine GIP<sub>10-30, 6-30, 7-30</sub> antagonistic peptides (Abstract).  
Porcine GIP<sub>7-30</sub> consist essentially of a 24 amino acid polypeptide corresponding to positions 7-30  
of the sequence of human GIP, SEQ ID NO:2. Porcine GIP<sub>10-30, 6-30, 7-30</sub> comprise at least an  
10        effective number of amino acids corresponding to those amino acids in the 7-30 positions of  
human or rat GIP, SEQ ID NO:2 or 8, respectively, or effective alternative sequences thereto.  
Porcine GIP<sub>6-30</sub> comprises at least an effective number of amino acids corresponding to those  
amino acids in the 7-30 positions of rat GIP, SEQ ID NO:8, or effective alternative sequences  
thereto. A chemical composition and its properties are inseparable. Therefore, the properties  
15        applicant discloses and/or claims, i.e. "interferes with the biological activity of GIP in an animal",  
are an inherent property of Porcine GIP<sub>10-30, 6-30, 7-30</sub>. Porcine GIP<sub>6-30</sub> is an effective alternative  
sequence to amino acids 16-30 of rat GIP, SEQ ID NO:9.

14.        Claims 1, 8-14, 18-41 are rejected under 35 U.S.C. 102(b) as being anticipated by Ebert  
(y12). Ebert teaches a specific GIP antiserum (page 1601, paragraph bridging columns 1-2). The

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antiserum comprises an antibody or antibodies that is or are an antagonist of GIP, consist essentially of or comprises a 24 amino acid polypeptide corresponding to any position of the sequence of GIP, or comprise at least an effective number of amino acids corresponding to those amino acids in any position of GIP or effective alternative sequences thereto because the metes and bounds of "corresponding to" are not clearly set forth and because there are no structural or functional limitations to "effective alternative sequences thereto". Ebert also teaches a pharmaceutical composition comprising the anti-GIP, antagonistic antibody or antibodies (page 1602, columns 1-2). Inhibiting, blocking, or reducing glucose adsorption from the intestine is an inherent property of the antibody or antibodies, absent any evidence to the contrary. The intended use of the claimed pharmaceutical composition has not been given patentable weight because the recitation occurs in the preamble.

### ***Claim Rejections - 35 USC § 103***

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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16. Claims 8, 15, 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gelling (x12) or Ebert (y12) as applied to claim 8 above, and further in view of Avis (z12) and/or Turco (uu12). Gelling or Ebert teach a GIP antagonist, as discussed above. Gelling or Ebert are silent with respect to a lyophilized and/or reconstituted GIP antagonist. Avis teaches that biologics and pharmaceuticals can be stored in the dry state in which there are relatively few stability problems (page 1565, paragraph bridging columns 1-2). Turco teaches that proper electrolyte concentration and balance in plasma and tissues are critical for proper body function and that the electrolytes in normal saline more closely approximate the composition of the extracellular fluid than solutions of any other single salt (page 1570, column 2, bottom). Avis and/or Turco are silent with respect to a lyophilized and/or reconstituted GIP antagonist. However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to make a GIP antagonist, as taught by Gelling or Ebert, and to modify that teaching by lyophilizing and/or reconstituting the antagonist, as taught by Avis and/or Turco, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to combine these teachings because there are relatively few stability problems in the dry state and because normal saline more closely approximates the composition of the extracellular fluid than solutions of any other single salt. The invention is prima facie obvious over the prior art.

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*Conclusion*

17. No claims are allowable.

18. This is a continuation of applicant's earlier Application No. 08984476. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.



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Any inquiry concerning this communication or earlier communications from the examiner should be directed to David S. Romeo whose telephone number is (703) 305-4050. The examiner can normally be reached on Monday through Friday from 6:45 a.m. to 3:15 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242.

Faxed draft or informal communications should be directed to the examiner at (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

  
David Romeo  
Primary Examiner  
August 31, 2000